

L Number	Hits	Search Text	DB	Time stamp
4	10	(method or administer?) with VEGF with (variant or mutant or mutation or agonist) with KDR	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:11
5	270	kdr adj receptor\$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:12
6	80	vegf adj variant	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:12
7	7	vegf adj receptor adj agonist	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:12
8	7	vegf adj receptor\$ adj agonist\$	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:13
9	554	(kdr adj receptor\$) smae (vegf adj variant) same (vegf adj receptor\$ adj agonist\$)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:13
10	0	(kdr adj receptor\$) same (vegf adj variant) same (vegf adj receptor\$ adj agonist\$)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:13
11	7	(kdr adj receptor\$) same ((vegf adj variant) or (vegf adj receptor adj agonist))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2004/06/14 12:13
15	87	vegf with (amino adj acid) with (substitution\$ or modification\$ or change\$ or conversion\$)	USPAT; US-PGPUB	2004/06/14 12:52
16	8	(d63s or d63 or asp63 or g65m or gly65 or g65 or l66r or leu66 or "l66") with vegf	USPAT; US-PGPUB	2004/06/14 12:55
17	6	(vegf adj variant) same (kdr adj receptor\$)	USPAT; US-PGPUB	2004/06/14 12:55
-	10	shen-ben\$.IN.	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 14:28
-	11	zioncheck-t\$.IN.	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:35
-	7452	vascular adj endothelial adj growth adj factor or vegf	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:36
-	215360	variant or agonist	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:37
-	579	(vascular adj endothelial adj growth adj factor or vegf) with (variant or agonist)	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:37
-	857	(vascular adj endothelial adj growth adj factor or vegf) same (variant or agonist)	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:37

-	220353	(treating or treatment or prevention or preventing) with (disease or disorder)	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:38
-	3	((treating or treatment or prevention or preventing) with (disease or disorder)) same ((vascular adj endothelial adj growth adj factor or vegf) same (variant or agonist))) and administer?	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:38
-	148	((treating or treatment or prevention or preventing) with (disease or disorder)) same ((vascular adj endothelial adj growth adj factor or vegf) same (variant or agonist))	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 12:12
-	1	"9820027"	USPAT; US-PGPUB	2003/12/10 11:49
-	2	barker-s\$.IN. and martin-j\$.IN.	USPAT; US-PGPUB	2003/12/10 11:50
-	6	barker-s\$.IN. and martin-j\$.IN.	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:52
-	2	5955311.PN.	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 11:52
-	34	((treating or treatment or prevention or preventing) with (disease or disorder)) same ((vascular adj endothelial adj growth adj factor or vegf) same (variant or agonist)) and (kinase adj domain adj region or kdr)	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 12:13
-	2	6020473.PN.	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 14:32
-	2	6057428.PN.	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 14:33
-	2	6592788.PN.	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 14:35
-	0	vegf adj mutagenesis	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 14:35
-	118	vegf same mutagenesis	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 14:35
-	5	"9708313"	USPAT; US-PGPUB; EPO; DERWENT	2003/12/10 14:35

09/700806 14/06/2004

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NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 8 MAR 03 FRANCEPAT now available on STN
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NEWS 13 APR 26 IFIPAT/IFIUDB/IFICDB: New super search and display field available
NEWS 14 APR 26 LITALERT now available on STN
NEWS 15 APR 27 NLDB: New search and display fields available
NEWS 16 May 10 PROUSDDR now available on STN
NEWS 17 May 19 PROUSDDR: One FREE connect hour, per account, in both May and June 2004
NEWS 18 May 12 EXTEND option available in structure searching
NEWS 19 May 12 Polymer links for the POLYLINK command completed in REGISTRY
NEWS 20 May 17 FRFULL now available on STN
NEWS 21 May 27 STN User Update to be held June 7 and June 8 at the SLA 2004 Conference
NEWS 22 May 27 New UPM (Update Code Maximum) field for more efficient patent SDIs in CAplus
NEWS 23 May 27 CAplus super roles and document types searchable in REGISTRY
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NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004

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FILE 'HOME' ENTERED AT 13:38:21 ON 14 JUN 2004

=> file medline caplus scisearch biosis uspatfull pctfull
COST IN U.S. DOLLARS SINCE FILE TOTAL
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CA INDEXING COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'PCTFULL' ENTERED AT 13:38:43 ON 14 JUN 2004
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=> s kdr(w) receptor?
L1 880 KDR(W) RECEPTOR?

=> s vegf(w) receptor(w) agonist?
L2 11 VEGF(W) RECEPTOR(W) AGONIST?

=> s vegf(3a)variant?
L3 777 VEGF (3A) VARIANT?

=> s 11(s)(l2 or l3)
L4 21 L1(S)(L2 OR L3)

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=> dup rem l4  
PROCESSING COMPLETED FOR L4  
L5          17 DUP REM L4 (4 DUPLICATES REMOVED)
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=> d ibib abs 1-17

L5 ANSWER 1 OF 17 USPATFULL on STN
ACCESSION NUMBER: 2004:44956 USPATFULL
TITLE: Use of VEGF for treating bone defects
INVENTOR(S): Bunting, Stuart, Half Moon Bay, CA, UNITED STATES
Carano, Richard, San Ramon, CA, UNITED STATES
Filvaroff, Ellen Hope, San Francisco, CA, UNITED STATES
Gosselin, Richard Andre, El Granada, CA, UNITED STATES
Peale, Franklin V., JR., San Carlos, CA, UNITED STATES
PATENT ASSIGNEE(S): GENENTECH, INC. (U.S. corporation)

09/700806 14/06/2004

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004033949 | A1 | 20040219 |
| APPLICATION INFO.: | US 2003-431105 | A1 | 20030506 (10) |

| | NUMBER | DATE |
|-----------------------|---|---------------|
| PRIORITY INFORMATION: | US 2002-378275P | 20020506 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA,
94080 | |
| NUMBER OF CLAIMS: | 31 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 7 Drawing Page(s) | |
| LINE COUNT: | 1650 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides pharmaceutical compositions comprising VEGF or variants thereof for promoting bone formation, in vitro and in vivo. Methods of using those compositions are also provided. Compositions and methods of the present invention can be used for promoting and improving the repair process in subjects with bone defects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 2 OF 17 USPATFULL on STN
ACCESSION NUMBER: 2004:103582 USPATFULL
TITLE: Medical articles prepared for cell adhesion
INVENTOR(S): Carlyle, Wenda C., Petaluma, CA, United States
Brendzel, Avrom M., Roseville, MN, United States
PATENT ASSIGNEE(S): St. Jude Medical, Inc., United States (U.S.
corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6726718 | B1 | 20040427 |
| APPLICATION INFO.: | US 1999-459451 | | 19991213 (9) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | GRANTED | | |
| PRIMARY EXAMINER: | Willse, David H. | | |
| ASSISTANT EXAMINER: | Blanco, Javier G. | | |
| LEGAL REPRESENTATIVE: | Altera Law Group, LLC, Finucane, Hallie A. | | |
| NUMBER OF CLAIMS: | 35 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 16 Drawing Figure(s); 16 Drawing Page(s) | | |
| LINE COUNT: | 1256 | | |

AB A prosthesis is formed from a biocompatible material having one or more associated cell adhesion stimulating proteins. The biocompatible material can be a ceramic material or a carbon coated material. The cell adhesion stimulating protein can be a structural protein or a polypeptide growth factor, such as vascular endothelial growth factor. Viable cells can be adhered in vivo or in vitro to the biocompatible material with the cell adhesion stimulating protein.

L5 ANSWER 3 OF 17 USPATFULL on STN
ACCESSION NUMBER: 2003:135058 USPATFULL
TITLE: Medical devices that stimulate growth factor production
INVENTOR(S): Ogle, Matthew F., Oronoco, MN, UNITED STATES
McConico, Andrea L., Fridley, MN, UNITED STATES

| | NUMBER | KIND | DATE |
|-----------------------|--|------|---------------|
| PATENT INFORMATION: | US 2003093147 | A1 | 20030515 |
| APPLICATION INFO.: | US 2001-8430 | A1 | 20011113 (10) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | PATTERSON, THUENTE, SKAAR & CHRISTENSEN, P.A., 4800 IDS CENTER, 80 SOUTH 8TH STREET, MINNEAPOLIS, MN, 55402-2100 | | |
| NUMBER OF CLAIMS: | 35 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 4 Drawing Page(s) | | |
| LINE COUNT: | 1356 | | |

AB Medical devices are described that have a releasable quantity of a stimulation compound that stimulates production of VEGF. The stimulation compound can be a polypeptide, such as hypoxia-inducible factor 1. Suitable stimulation compounds stimulate transcription of VEGF. Medical devices of particular interest include, for example, heart valve prostheses, vascular prostheses and vascular stents.

L5 ANSWER 4 OF 17 USPATFULL on STN
 ACCESSION NUMBER: 2003:128022 USPATFULL
 TITLE: Treatment protocol generation for diseases related to angiogenesis
 INVENTOR(S): Agur, Zvia, Tel Aviv, ISRAEL
 Arakelyan, Levon, Ashdod, ISRAEL
 Vainstein, Vladimir, Jerusalem, ISRAEL

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2003088237 | A1 | 20030508 |
| APPLICATION INFO.: | US 2002-207772 | A1 | 20020731 (10) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2001-330929P | 20011102 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | SUGHRUE MION, PLLC, 2100 Pennsylvania Avenue, N.W., Washington, DC, 20037-3213 | |
| NUMBER OF CLAIMS: | 40 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 13 Drawing Page(s) | |
| LINE COUNT: | 1023 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A computer-implemented method for determining an optimal treatment protocol for a disease related to angiogenesis, comprising creating an angiogenesis model including pro-angiogenesis and anti-angiogenesis factors. Effective vessel density (EVD) is incorporated as a factor regulating switching on and switching off of at least one component in the angiogenesis model. Effects of vasculature maturation and mature vessels destabilization are incorporated. Pro-angiogenesis and anti-angiogenesis factors, which can influence changes in state of a tissue are selected. Effects of drugs in the pro-angiogenesis and anti-angiogenesis factors are incorporated. A plurality of treatment protocols in a protocol space is generated. A best treatment protocol based on a pre-determined criteria.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 5 OF 17 USPATFULL on STN
 ACCESSION NUMBER: 2003:38104 USPATFULL
 TITLE: VEGF fusion proteins
 INVENTOR(S): Kovesdi, Imre, Rockville, MD, UNITED STATES
 Kessler, Paul D., Frederick, MD, UNITED STATES
 PATENT ASSIGNEE(S): GenVec, Inc., Gaithersburg, MD, UNITED STATES, 20878
 (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|------|--------------|
| PATENT INFORMATION: | US 2003027751 | A1 | 20030206 |
| APPLICATION INFO.: | US 2001-832355 | A1 | 20010410 (9) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | LEYDIG VOIT & MAYER, LTD, TWO PRUDENTIAL PLAZA, SUITE 4900, 180 NORTH STETSON AVENUE, CHICAGO, IL, 60601-6780 | | |
| NUMBER OF CLAIMS: | 46 | | |
| EXEMPLARY CLAIM: | 1 | | |
| LINE COUNT: | 7034 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention provides therapeutic fusion proteins which include a first peptide portion comprising a first non-heparin binding VEGF peptide portion and a second non-VEGF peptide portion covalently associated with the first peptide portion, which first and second peptide portions separately promote angiogenesis, bone growth, wound healing, or any combination thereof. Further provided are polynucleotides encoding such fusion proteins, vectors including such polynucleotides, methods of making such proteins, and methods of promoting angiogenesis, bone growth, and/or wound healing using such proteins, polynucleotides, and vectors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 6 OF 17 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2003103581 PCTFULL ED 20040102 EW 200351
 TITLE (ENGLISH): COMPOSITIONS AND METHODS FOR LIVER GROWTH AND LIVER PROTECTION
 TITLE (FRENCH): COMPOSITIONS ET METHODES DE CROISSANCE ET DE PROTECTION DU FOIE
 INVENTOR(S): FERRARA, Napoleone, 2090 Pacific Avenue, #704, San Franicsco, CA 94109, US [US, US]; HILLAN, Kenneth, J., 64 Seward Street, San Francisco, CA 94114, US [GB, US]; LE COUTER, Jennifer, 585 Page Street, Apt. #1, San Francisco, CA 94117, US [CA, US]
 PATENT ASSIGNEE(S): GENENTECH, INC., 1 DNA Way, South San Francisco, CA 94080-4990, US [US, US], for all designates States except US;
 FERRARA, Napoleone, 2090 Pacific Avenue, #704, San Franicsco, CA 94109, US [US, US], for US only; HILLAN, Kenneth, J., 64 Seward Street, San Francisco, CA 94114, US [GB, US], for US only; LE COUTER, Jennifer, 585 Page Street, Apt. #1, San Francisco, CA 94117, US [CA, US], for US only
 AGENT: CUI, Steven X.\$, Genentech, Inc., 1 DNA Way, South San Francisco, CA 94080-4990\$, US
 LANGUAGE OF FILING: English
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| | NUMBER | KIND | DATE |
|----------------------|--|---|----------|
| DESIGNATED STATES | WO 2003103581 | A2 | 20031218 |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE
SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM
ZW | | |
| RW (ARIPO) : | GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW | | |
| RW (EAPO) : | AM AZ BY KG KZ MD RU TJ TM | | |
| RW (EPO) : | AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
MC NL PT RO SE SI SK TR | | |
| RW (OAPI) : | BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG | | |
| APPLICATION INFO.: | WO 2003-US17591 | A | 20030605 |
| PRIORITY INFO.: | US 2002-60/386,637 | | 20020605 |
| ABEN | The present invention provides pharmaceutical compositions and methods for liver proliferation and protection. Specifically useful are VEGFR modulating agents capable of promoting liver growth. Disclosed compositions and methods may be useful for promoting proliferation or treating pathological conditions in other organs of significant biological functions. | | |
| ABFR | L'invention concerne des compositions pharmaceutiques ainsi que des methodes de regeneration et de protection du foie. Plus particulierement, l'invention fait intervenir des agents de modulation du facteur de croissance vasculaire endotheliales (VEGFR) qui sont capables d'activer la croissance du foie. Les compositions et les methodes de l'invention peuvent servir a activer la regeneration ou a traiter des etats pathologiques dans d'autres organes qui remplissent d'importantes fonctions biologiques. | | |
| L5 | ANSWER 7 OF 17 | PCTFULL COPYRIGHT 2004 Univentio on STN | |
| ACCESSION NUMBER: | 2003094617 PCTFULL ED 20031125 EW 200347 | | |
| TITLE (ENGLISH) : | USE OF VEGF FOR TREATING BONE DEFECTS | | |
| TITLE (FRENCH) : | UTILISATION DE VEGF POUR TRAITER DES DEFAUTS OSSEUX | | |
| INVENTOR(S) : | BUNTING, Stuart, 220 Miramontes Avenue, Half Moon Bay, CA 94019, US;
FILVAROFF, Ellen Hope, 538 18th Avenue, San Francisco, CA 94121, US;
PEALE, Jr., Franklin V., 416 Pearl Avenue, San Carlos, CA 94070, US;
CARANO, Richard, 2470 Paddock Drive, San Ramon, CA 94583, US;
GOSSELIN, Richard Andre, 643 Ferdinand Avenue, El Granada, CA 94018, US | | |
| PATENT ASSIGNEE(S) : | GENENTECH, INC., 1 DNA Way, South San Francisco, CA 94080-4990, US [US, US] | | |
| AGENT: | CUI, Steven X.S., GENENTECH, INC., 1 DNA Way, South San Francisco, CA 94080-4990\$, US | | |
| LANGUAGE OF FILING: | English | | |
| LANGUAGE OF PUBL.: | English | | |
| DOCUMENT TYPE: | Patent | | |
| PATENT INFORMATION: | NUMBER | KIND | DATE |
| | WO 2003094617 | A2 | 20031120 |
| DESIGNATED STATES | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD | | |
| W: | | | |

MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE
 SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
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 RW (EPO) : AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
 MC NL PT RO SE SI SK TR
 RW (OAPI) : BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
 APPLICATION INFO. : WO 2003-US14090 A 20030506
 PRIORITY INFO. : US 2002-60/378,275 20020506

ABEN The present invention provides pharmaceutical compositions comprising VEGF or variants thereof for promoting bone formation, *< i>in vitro</i>* and *< i>in vivo</i>*. Methods of using those compositions are also provided. Compositions and methods of the present invention can be used for promoting and improving the repair process in subjects with bone defects.

ABFR L'invention concerne des compositions pharmaceutiques comprenant VEGF ou ses variants, lesquelles compositions permettant de favoriser la formation osseuse, *< i>in vitro</i>* et *< i>in vivo</i>*. L'invention concerne des methodes d'utilisation de ces compositions. Les compositions et les methodes de l'invention peuvent etre utilisees pour favoriser et pour ameliorer le processus de reparation chez des sujets presentant des defauts osseux.

L5 ANSWER 8 OF 17 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2003036410 PCTFULL ED 20030512 EW 200318
 TITLE (ENGLISH) : TREATMENT PROTOCOL GENERATION FOR DISEASES RELATED TO ANGIOGENESIS
 TITLE (FRENCH) : CREATION D'UN PROTOCOLE DE TRAITEMENT DE MALADIES ASSOCIEES A L'ANGIOGENESE
 INVENTOR(S) : AGUR, Zvia, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL];
 ARAKELYAN, Levon, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL];
 VAINSTEIN, Vladimir, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL]
 PATENT ASSIGNEE(S) : OPTIMATA LTD., Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL], for all designates States except US;
 AGUR, Zvia, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL], for US only;
 ARAKELYAN, Levon, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL], for US only;
 VAINSTEIN, Vladimir, Tuval St, 11, 52522 Ramat-Gan, IL [IL, IL], for US only
 AGENT: OPTIMATA LTD.\$, c/o MANDIR, William, H., Sughrue Mion, PLLC, 2100 Pennsylvania Ave., NW, Suite 800, Washington, DC 20073-3213\$, US
 LANGUAGE OF FILING: English
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| | NUMBER | KIND | DATE |
|-------------------|--|------|----------|
| DESIGNATED STATES | WO 2003036410 | A2 | 20030501 |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW | | |
| RW (ARIPO) : | AM AZ BY KG KZ MD RU TJ TM | | |
| RW (EAPO) : | AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC | | |
| RW (EPO) : | | | |

NL PT SE SK TR
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
 APPLICATION INFO.: WO 2002-IB4725 A 20021024
 PRIORITY INFO.: US 2001-60/330,592 20011025
 US 2002-10/207,772 20020731

ABEN A computer-implemented method for determining an optimal treatment protocol for a disease related to angiogenesis, comprising creating an angiogenesis model including pro-angiogenesis and anti-angiogenesis factors. Effective vessel density (EVD) is incorporated as a factor regulating switching on and switching off of at least one component in the angiogenesis model. Effects of vasculature maturation and mature vessels destabilization are incorporated. Pro-angiogenesis and anti-angiogenesis factors, which can influence changes in state of a tissue are selected. Effects of drugs in the pro-angiogenesis and anti-angiogenesis factors are incorporated. A plurality of treatment protocols in a protocol space is generated. A best treatment protocol based on a pre-determined criteria.

ABFR L'invention concerne un procede mis en oeuvre par ordinateur pour determiner un protocole de traitement optimal d'une maladie associee a l'angiogenese, qui consiste a creer un modele angiogenique comprenant des facteurs pro-angiogenese et des facteurs anti-angiogenese. Une densite effective des vaisseaux (EVD) est prise en compte en tant que facteur regulant la mise en service ou hors service d'au moins un element du modele angiogenique. Des effets de maturation du systeme vasculaire et de destabilisation des vaisseaux matures sont pris en compte. Des facteurs pro-angiogenese et des facteurs anti-angiogenese sont choisis, qui peuvent influer sur les changements d'etat d'un tissu. Les effets de medicaments sur les facteurs pro-angiogenese et les facteurs anti-angiogenese sont pris en compte. Plusieurs protocoles de traitement sont crees dans un espace de protocole. Un meilleur protocole de traitement est choisi sur la base de criteres preetablis.

L5 ANSWER 9 OF 17 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2002083851 PCTFULL ED 20021107 EW 200243
 TITLE (ENGLISH): VEGF FUSION PROTEINS
 TITLE (FRENCH): PROTEINES DE FUSION VEGF
 INVENTOR(S): KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855,
 US [US, US];
 KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD
 21701, US [US, US]
 PATENT ASSIGNEE(S): GENVEC, INC., 65 West Watkins Mill Road, Gaithersburg,
 MD 20878, US [US, US], for all designates States except
 US;
 KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855,
 US [US, US], for US only;
 KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD
 21701, US [US, US], for US only
 AGENT: SMITH, Len, S.S., Leydig, Voit & Mayer, Ltd., Suite
 4900, Two Prudential Plaza, 180 North Stetson, Chicago,
 IL 60601-6780\$, US
 LANGUAGE OF FILING: English
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| ----- | | |
| WO 2002083851 | A2 | 20021024 |

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
 CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD

MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI

SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

RW (ARIPO) : GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO) : AM AZ BY KG KZ MD RU TJ TM

RW (EPO) : AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
TR

RW (OAPI) : BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-US11406 A 20020410

PRIORITY INFO.: US 2001-09/832,355 20010410

ABEN The invention provides therapeutic fusion proteins which include a first peptide portion comprising a first non-heparin binding VEGF peptide portion and a second non-VEGF peptide portion covalently associated with the first peptide portion, which first and second peptide portions separately promote angiogenesis, bone growth, wound healing, or any combination thereof. Further provided are polynucleotides, encoding such fusion proteins, vectors including such polynucleotides, methods of making such proteins, and methods of promoting angiogenesis, bone growth, and/or wound healing using such proteins, polynucleotides, and vectors.

ABFR L'invention concerne des protéines de fusion thérapeutiques comprenant une première partie peptidique renfermant une première partie de peptide VEGF de liaison non heparinique et une seconde partie de peptide non VEGF associée par covalence à la première partie de peptide, lesdites première et seconde parties de peptide favorisant séparément l'angiogenèse, la croissance osseuse, la cicatrisation des blessures ou toute combinaison associée. L'invention concerne en outre des polynucléotides codant pour ces protéines de fusion, des vecteurs comprenant ces polynucléotides, des méthodes de fabrication de ces protéines ainsi que des méthodes destinées à favoriser l'angiogenèse, la croissance osseuse et/ou la cicatrisation des blessures au moyen de ces protéines, ces polynucléotides et ces vecteurs.

L5 ANSWER 10 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2001:338563 CAPLUS

DOCUMENT NUMBER: 134:348629

TITLE: Modulation of eNOS activity using VEGF, a variant, or VEGF receptor agonists and therapeutic uses thereof

INVENTOR(S) : Shen, Ben-Quan; Zioncheck, Thomas

PATENT ASSIGNEE(S) : Genentech, Inc., USA

SOURCE: PCT Int. Appl., 71 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|-------|----------|-----------------|----------|
| ----- | ----- | ----- | ----- | ----- |
| WO 2001032695 | A2 | 20010510 | WO 2000-US30294 | 20001102 |
| WO 2001032695 | A3 | 20020214 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1225910 A2 20020731 EP 2000-980281 20001102

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003513105 T2 20030408 JP 2001-535394 20001102
PRIORITY APPLN. INFO.: US 1999-163132P P 19991102
WO 2000-US30294 W 20001102

AB The present invention provides uses of VEGF, a variant, or VEGF receptor agonists for the up-regulation of eNOS expression and activity. VEGF, its variants, and VEGF receptor agonists are useful in the treatment of or prevention from hypertension, diabetes, angina, thrombosis, atherosclerosis, heart failure, and other conditions or disorders wherein nitric oxide is an important regulator. Methods of preparing the variants are also disclosed in the patent.

L5 ANSWER 11 OF 17 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 2001:378043 SCISEARCH

THE GENUINE ARTICLE: 428WH

TITLE: Vascular endothelial growth factor KDR receptor signaling potentiates tumor necrosis factor-induced tissue factor expression in endothelial cells

AUTHOR: Shen B Q; Lee D Y; Cortopassi K M; Damico L A; Zioncheck T F (Reprint)

CORPORATE SOURCE: Genentech Inc, Dept Metab & Pharmacokinet, MS 70, 1 DNA Way, S San Francisco, CA 94080 USA (Reprint); Genentech Inc, Dept Metab & Pharmacokinet, S San Francisco, CA 94080 USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (16 FEB 2001) Vol. 276, No. 7, pp. 5281-5286.

Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.

ISSN: 0021-9258.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 54

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Vascular endothelial growth factor (VEGF) and tumor necrosis factor-alpha (TNF-alpha) have been shown to synergistically increase tissue factor (TF) expression in endothelial cells; however, the role of the VEGF receptors (KDR, Flt-1, and neuropilin) in this process is unclear. Here we report that VEGF binding to the **KDR receptor** is necessary and sufficient for the potentiation of TNF-induced TF expression in human umbilical vein endothelial cells. TF expression was evaluated by Western blot analysis and fluorescence-activated cell sorting. In the absence of TNF-alpha, wild-type VEGF- or **KDR receptor**-selective variants induced an approximate 7-fold increase in total TF expression. Treatment with TNF alone produced an approximate 110-fold increase in total TF expression, whereas coincubation of TNF-alpha with wild-type **VEGF**- or KDR-selective **variants** resulted in an approximate 250-fold increase in TF expression. VEGF lacking the heparin binding domain was also able to potentiate TF expression, indicating that heparin-sulfate proteoglycan or neuropilin binding is not required for TF up-regulation. Neither placental growth factor nor an Flt-1-selective variant was capable of inducing TF expression in the presence or absence of TNF. Inhibition of protein-tyrosine kinase or protein kinase C activity significantly blocked the TNF/VEGF potentiation of TF up-regulation, whereas phorbol 12-myristate 13-acetate, a protein kinase C activator, increased TF expression. These data demonstrate that **KDR receptor** signaling governs both VEGF-induced TF expression and the potentiation of TNF-induced up-regulation of TF.

L5 ANSWER 12 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2000:756863 CAPLUS
 DOCUMENT NUMBER: 133:318304
 TITLE: Vascular endothelial cell growth factor (VEGF)
 variants and pharmaceutical uses thereof
 INVENTOR(S): Cunningham, Brian; Abraham, Devos; Li, Bing
 PATENT ASSIGNEE(S): Genentech, Inc., USA
 SOURCE: PCT Int. Appl., 70 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2000063380 | A1 | 20001026 | WO 2000-US9483 | 20000410 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1171594 | A1 | 20020116 | EP 2000-921966 | 20000410 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO | | | | |
| JP 2002541849 | T2 | 20021210 | JP 2000-612459 | 20000410 |
| NZ 514488 | A | 20040130 | NZ 2000-514488 | 20000410 |
| AU 771042 | B2 | 20040311 | AU 2000-42220 | 20000410 |
| PRIORITY APPLN. INFO.: | | | US 1999-129788P | P 19990416 |
| | | | US 2000-184235P | P 20000223 |
| | | | WO 2000-US9483 | W 20000410 |

AB The present invention provides **VEGF variants** having at least a single amino acid mutation in the native VEGF sequence and selective binding affinity for either the kinase domain region (**KDR**) receptor or the FMS-like tyrosine kinase region (**FLT-1**) receptor. Methods of making the VEGF variants and methods of using the VEGF variants are also provided. The VEGF variants may have pharmaceutical applications. Only sequence #1, 2, 7, 8 are claimed.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
 ACCESSION NUMBER: 2000:716110 CAPLUS
 DOCUMENT NUMBER: 133:291561
 TITLE: Vascular endothelial growth factor C (VEGF-C)
 ΔCys156 protein and gene, and uses thereof
 INVENTOR(S): Alitalo, Kari; Joukov, Vladimir
 PATENT ASSIGNEE(S): Helsinki University Licensing, Ltd., Finland
 SOURCE: U.S., 87 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 12
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| US 6130071 | A | 20001010 | US 1997-795430 | 19970205 |

| | | | | |
|--|----|----------|----------------|----------|
| WO 9833917 | A1 | 19980806 | WO 1998-US1973 | 19980202 |
| W: AU, CA, CN, JP, NZ, US, US, US, US, US, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9862624 | A1 | 19980825 | AU 1998-62624 | 19980202 |
| AU 748369 | B2 | 20020606 | | |
| EP 972028 | A1 | 20000119 | EP 1998-904842 | 19980202 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, FI | | | | |
| JP 2001523951 | T2 | 20011127 | JP 1998-533178 | 19980202 |
| US 6361946 | B1 | 20020326 | US 1999-355700 | 19991105 |
| AU 755708 | B2 | 20021219 | AU 2000-10072 | 20000113 |
| US 2003091567 | A1 | 20030515 | US 2002-201386 | 20020723 |
| PRIORITY APPLN. INFO.: | | | | |
| US 1994-340011 A2 19941114 | | | | |
| US 1995-510133 A2 19950801 | | | | |
| US 1996-585895 A2 19960112 | | | | |
| US 1996-601132 A2 19960214 | | | | |
| US 1996-671573 A2 19960628 | | | | |
| AU 1996-66169 A3 19960801 | | | | |
| WO 1996-FI427 A2 19960801 | | | | |
| US 1997-795430 A2 19970205 | | | | |
| WO 1998-US1973 W 19980202 | | | | |
| US 1999-355700 A1 19991105 | | | | |
| US 2000-534376 A1 20000324 | | | | |

AB Provided are purified and isolated **VEGF-C** cysteine deletion **variants** that bind to Flt4 receptor tyrosine kinase (VEGFR-3) but demonstrate reduced binding (relative to VEGF-C) to **kdr** receptor tyrosine kinase (VEGFR-2); polynucleotides encoding the polypeptide; vectors and host cells that embody the polynucleotides; pharmaceutical compns. and diagnostic reagents comprising the polypeptides; and methods of making and using the foregoing. The variants are expected to have the same biol. activities as VEGF-C (including but not limited to affecting growth and migration of vascular endothelial cells; promoting growth of lymphatic endothelial cells and lymphatic vessels; increasing vascular permeability; and affecting myelopoiesis) support numerous diagnostic and in vitro and in vivo clin. utilities for polypeptides and antibodies of the invention, for modulating (stimulating or inhibiting) these biol. activities.

REFERENCE COUNT: 210 THERE ARE 210 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 14 OF 17 USPATFULL on STN

ACCESSION NUMBER: 2000:54211 USPATFULL
 TITLE: Variants of vascular endothelial cell growth factor
 INVENTOR(S): Keyt, Bruce A., Pacifica, CA, United States
 Nguyen, Francis Hung, Daly City, CA, United States
 Ferrara, Napoleone, San Francisco, CA, United States
 Cunningham, Brian C., San Mateo, CA, United States
 Wells, James A., Burlingame, CA, United States
 Li, Bing, Foster City, CA, United States
 Genentech, Inc., S. San Francisco, CA, United States
 (U.S. corporation)

| PATENT INFORMATION: | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6057428 | | 20000502 |
| APPLICATION INFO.: | US 1996-691794 | | 19960802 (8) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1995-567200, filed on 5 Dec 1995 | | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |

PRIMARY EXAMINER: Feisee, Lila
ASSISTANT EXAMINER: Kaufman, Claire M.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 27 Drawing Figure(s); 24 Drawing Page(s)
LINE COUNT: 3120

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 15 OF 17 USPATFULL on STN
ACCESSION NUMBER: 2000:12936 USPATFULL
TITLE: Nucleic acids encoding variants of vascular endothelial cell growth factor
INVENTOR(S): Keyt, Bruce A., Pacifica, CA, United States
Nguyen, Francis Hung, Daly City, CA, United States
Ferrara, Napoleone, San Francisco, CA, United States
PATENT ASSIGNEE(S): Genentech, Inc., S. San Francisco, CA, United States
(U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|---|---------|--------------|
| PATENT INFORMATION: | US 6020473 | | 20000201 |
| APPLICATION INFO.: | US 1995-567200 | | 19951205 (8) |
| DOCUMENT TYPE: | | Utility | |
| FILE SEGMENT: | | Granted | |
| PRIMARY EXAMINER: | Spector, Lorraine | | |
| ASSISTANT EXAMINER: | Kaufman, Claire M. | | |
| LEGAL REPRESENTATIVE: | Johnston, Sean, Vance, Dolly A. Flehr Hohbach Test
Albritton & Herbert LLP | | |
| NUMBER OF CLAIMS: | 8 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 23 Drawing Figure(s); 21 Drawing Page(s) | | |
| LINE COUNT: | 2668 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 16 OF 17 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:696070 CAPLUS
DOCUMENT NUMBER: 133:305707

TITLE: Receptor-selective variants of human vascular endothelial growth factor: generation and characterization
AUTHOR(S): Li, Bing; Fuh, Germaine; Meng, Gloria; Xin, Xiaohua; Gerritsen, Mary E.; Cunningham, Brian; De Vos, Abraham M.
CORPORATE SOURCE: Department of Protein Engineering, Genentech, Inc., South San Francisco, CA, 94080, USA
SOURCE: Journal of Biological Chemistry (2000), 275(38), 29823-29828
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Vascular endothelial growth factor (VEGF) is a pleiotropic factor that exerts a multitude of biol. effects through its interaction with two receptor tyrosine kinases, fms-like tyrosine kinase (Flt-1) or VEGF receptor 1 and kinase insert domain-containing receptor (KDR) or VEGF receptor 2. Whereas it is commonly accepted that KDR is responsible for the proliferative activities of VEGF, considerable controversy and uncertainty exist about the role of the individual receptors in eliciting many of the other effects. Based on a comprehensive mutational anal. of the receptor-binding site of VEGF, an Flt-1-selective variant was created containing four substitutions from the wild-type protein. This variant bound with wild-type affinity to Flt-1, was at least 470-fold reduced in binding to KDR, and had no activity in cell-based assays measuring autophosphorylation of KDR or proliferation of primary human vascular endothelial cells. Using a competitive phage display strategy, two KDR-selective variants were discovered with three and four changes from wild-type, resp. Both variants had approx. wild-type affinity for KDR, were about 2000-fold reduced in binding to Flt-1, and showed activity comparable with the wild-type protein in KDR autophosphorylation and endothelial cell proliferation assays. These variants will serve as useful reagents in elucidating the roles of Flt-1 and KDR.
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 17 OF 17 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 1998016551 PCTFULL ED 20020514
TITLE (ENGLISH): VARIANTS OF VASCULAR ENDOTHELIAL CELL GROWTH FACTOR HAVING ANTAGONISTIC PROPERTIES
TITLE (FRENCH): VARIANTS DE FACTEUR DE CROISSANCE DE CELLULES ENDOTHELIALES VASCULAIRES POSSEDANT DES PROPRIETES ANTAGONISTES
INVENTOR(S): KEYT, Bruce, A.; NGUYEN, Francis, Hung; FERRARA, Napoleone
PATENT ASSIGNEE(S): GENENTECH, INC.; KEYT, Bruce, A.; NGUYEN, Francis, Hung; FERRARA, Napoleone
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:
NUMBER KIND DATE

WO 9816551 A2 19980423
DESIGNATED STATES
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI GB GE GH HU ID IL IS JP KE KG KP KR KZ LC LK LR

LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE
SG SI SK SL TJ TM TR TT UA UG US UZ VN YU ZW GH KE LS
MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH DE
DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI
CM GA GN ML MR NE SN TD TG

APPLICATION INFO.: WO 1997-US19471 A 19971010

PRIORITY INFO.: US 1996-8/734,443 19961017

ABEN The present invention involves the preparation of vascular endothelial growth factor (VEGF) antagonist molecules comprising variant VEGF polypeptides which are capable of binding to and occupying cell surface VEGF receptors without inducing a VEGF response, thereby antagonizing the biological activity of the native VEGF protein. Specifically, the variant VEGF polypeptides of the present invention comprise modifications of at least one cysteine residue in the native VEGF sequence, thereby inhibiting the ability of the variant polypeptide to dimerize through the formation of disulfide bonds. The present invention is further directed to methods for preparing such variant VEGF antagonists and to methods, compositions and assays utilizing such variants for producing pharmaceutically active materials having therapeutic and pharmacologic properties that differ from the native VEGF protein.

ABFR L'invention concerne la preparation de molecules antagonistes du facteur de croissance endotheliaire vasculaire (VEGF) comprenant des variants de polypeptides de VEGF capables de se lier aux recepteurs de VEGF a la surface des cellules et de les occuper sans produire une reponse VEGF, ayant ainsi un effet antagoniste sur l'activite biologique de la proteine de VEGF native. En particulier, les variants de polypeptides de VEGF faisant l'objet de la presente invention comprennent des modifications d'au moins un residu de cysteine dans la sequence de VEGF native, inhibant ainsi la capacite du variant de polypeptide a dimeriser par formation de ponts disulfures. La presente invention prevoit egalement des procedes de preparation de tels variants d'antagonistes du VEGF ainsi que des procedes, des compositions et des analyses pour lesquels on utilise de tels variants en vue de produire des matieres pharmaceutiquement actives possedant des proprietes therapeutiques et pharmacologiques qui different de la proteine de VEGF native.

=> d his

(FILE 'HOME' ENTERED AT 13:38:21 ON 14 JUN 2004)

FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS, USPATFULL, PCTFULL' ENTERED AT 13:38:43 ON 14 JUN 2004

L1 880 S KDR(W)RECEPTOR?
L2 11 S VEGF(W)RECEPTOR(W)AGONIST?
L3 777 S VEGF(3A)VARIANT?
L4 21 S L1(S) (L2 OR L3)
L5 17 DUP REM L4 (4 DUPLICATES REMOVED)

09/700806 14/06/2004

=> s amino(w)acid(w)(substitution? or change? or convert? or mutated or mutation) (w)vegf
2 FILES SEARCHED...
5 FILES SEARCHED...

L6 230 AMINO(W) ACID(W)(SUBSTITUTION? OR CHANGE? OR CONVERT? OR MUTATED
OR MUTATION) (W) VEGF

=> s (d63s or g65m or l66r or asp63 or d63 or gly65 or g65 or leu66 or 166) (s)vegf
L66 NOT FOUND

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of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s (d63s or g65m or l66r or asp63 or d63 or gly65 or g65 or leu66) (s)vegf
L7 29 (D63S OR G65M OR L66R OR ASP63 OR D63 OR GLY65 OR G65 OR LEU66) (S)
VEGF

=> dup rem 17
PROCESSING COMPLETED FOR L7
L8 27 DUP REM L7 (2 DUPLICATES REMOVED)

=> d his

(FILE 'HOME' ENTERED AT 13:38:21 ON 14 JUN 2004)

FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS, USPATFULL, PCTFULL' ENTERED AT
13:38:43 ON 14 JUN 2004

L1 880 S KDR(W)RECEPTOR?
L2 11 S VEGF(W)RECEPTOR(W)AGONIST?
L3 777 S VEGF(3A)VARIANT?
L4 21 S L1(S) (L2 OR L3)
L5 17 DUP REM L4 (4 DUPLICATES REMOVED)
L6 230 S AMINO(W)ACID(W)(SUBSTITUTION? OR CHANGE? OR CONVERT? OR MUTAT
L7 29 S (D63S OR G65M OR L66R OR ASP63 OR D63 OR GLY65 OR G65 OR LEU6
L8 27 DUP REM L7 (2 DUPLICATES REMOVED)

=> s 18 and 16 and 11
L9 0 L8 AND L6 AND L1

=> s 18 and 11
L10 16 L8 AND L1

=> d ibib abs 1-16

L10 ANSWER 1 OF 16 USPATFULL on STN
ACCESSION NUMBER: 2004:88227 USPATFULL
TITLE: Targeted therapeutic lipid constructs
INVENTOR(S): Brunke, Karen J., Belmont, CA, UNITED STATES
Wartchow, Charles A., San Francisco, CA, UNITED STATES
Cleland, Jeffrey L., San Carlos, CA, UNITED STATES

| | NUMBER | KIND | DATE |
|-----------------------|---|------|---------------|
| PATENT INFORMATION: | US 2004067196 | A1 | 20040408 |
| APPLICATION INFO.: | US 2003-401280 | A1 | 20030327 (10) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. US 2001-976254, filed
on 11 Oct 2001, PENDING | | |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | US 2000-239684P | 20001011 (60) |
| | US 2002-367858P | 20020327 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: SWANSON & BRATSCHUN L.L.C., 1745 SHEA CENTER DRIVE,
SUITE 330, HIGHLANDS RANCH, CO, 80129

NUMBER OF CLAIMS: 15
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 2 Drawing Page(s)
LINE COUNT: 2334

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel therapeutic lipid constructs comprising a lipid construct, an anti-cell surface targeting agent, and a radiotherapeutic metal ion are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 2 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2004:44956 USPATFULL
TITLE: Use of VEGF for treating bone defects
INVENTOR(S): Bunting, Stuart, Half Moon Bay, CA, UNITED STATES
Carano, Richard, San Ramon, CA, UNITED STATES
Filvaroff, Ellen Hope, San Francisco, CA, UNITED STATES
Gosselin, Richard Andre, El Granada, CA, UNITED STATES
Peale, Franklin V., JR., San Carlos, CA, UNITED STATES
PATENT ASSIGNEE(S): GENENTECH, INC. (U.S. corporation)

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|---------------|
| PATENT INFORMATION: | US 2004033949 | A1 | 20040219 |
| APPLICATION INFO.: | US 2003-431105 | A1 | 20030506 (10) |

| | NUMBER | DATE |
|-----------------------|-----------------|---------------|
| PRIORITY INFORMATION: | US 2002-378275P | 20020506 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: GENENTECH, INC., 1 DNA WAY, SOUTH SAN FRANCISCO, CA, 94080
NUMBER OF CLAIMS: 31
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 1650

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention provides pharmaceutical compositions comprising VEGF or variants thereof for promoting bone formation, in vitro and in vivo. Methods of using those compositions are also provided. Compositions and methods of the present invention can be used for promoting and improving the repair process in subjects with bone defects.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 3 OF 16 USPATFULL on STN

ACCESSION NUMBER: 2003:119619 USPATFULL
TITLE: Targeted therapeutic lipid constructs having cell surface targets
INVENTOR(S): Wartchow, Charles Aaron, San Carlos, CA, UNITED STATES
Pease, John S., Los Altos, CA, UNITED STATES
Shen, Zhi Min, Palo Alto, CA, UNITED STATES
PATENT ASSIGNEE(S): TARGESOME, INC. (U.S. corporation)

| | NUMBER | KIND | DATE |
|--|--------|------|------|
|--|--------|------|------|

PATENT INFORMATION: US 2003082103 A1 20030501
 APPLICATION INFO.: US 2002-262576 A1 20021001 (10)
 RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-976254, filed
 on 11 Oct 2001, PENDING

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2000-239684P | 20001011 (60) |
| | US 2001-326310P | 20011001 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | SWANSON & BRATSCHUN L.L.C., 1745 SHEA CENTER DRIVE,
SUITE 330, HIGHLANDS RANCH, CO, 80129 | |
| NUMBER OF CLAIMS: | 32 | |
| EXEMPLARY CLAIM: | 1 | |
| NUMBER OF DRAWINGS: | 2 Drawing Page(s) | |
| LINE COUNT: | 2294 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel therapeutic lipid constructs comprising a polymerized liposome, an anti-cell surface targeting agent, and a radiotherapeutic metal ion are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 4 OF 16 USPATFULL on STN
 ACCESSION NUMBER: 2002:112878 USPATFULL
 TITLE: Ligand for vascular endothelial growth factor receptor
 INVENTOR(S): Tchistiakova, Lioudmila, Laval, CANADA
 Li, Shengmin, Laval, CANADA
 Pietrzynski, Grzegorz, Montreal, CANADA
 Alakhov, Valery, Baie d'Urfe, CANADA

| | NUMBER | KIND | DATE |
|---------------------|----------------|------|--------------|
| PATENT INFORMATION: | US 2002058619 | A1 | 20020516 |
| | US 6733755 | B2 | 20040511 |
| APPLICATION INFO.: | US 2001-775743 | A1 | 20010202 (9) |

| | NUMBER | DATE |
|-----------------------|--|---------------|
| PRIORITY INFORMATION: | US 2000-180568P | 20000204 (60) |
| DOCUMENT TYPE: | Utility | |
| FILE SEGMENT: | APPLICATION | |
| LEGAL REPRESENTATIVE: | GIBBONS, DEL DEO, DOLAN, GRIFFINGER & VECCHIONE, 1
RIVERFRONT PLAZA, NEWARK, NJ, 07102-5497 | |
| NUMBER OF CLAIMS: | 24 | |
| EXEMPLARY CLAIM: | 1 | |
| LINE COUNT: | 3407 | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to compositions comprised of a peptide ligand or derivatives thereof that are capable of specific binding to the high affinity receptor-1 of vascular endothelial growth factor (VEGF) and structure similar receptors. The invention further provides a peptide ligand or derivatives thereof that are capable of inhibiting angiogenesis induced by VEGF. The present invention also provides a method for treatment or diagnosis of disease associated with angiogenesis in a patient in need of therapy comprising administering to the patient an effective amount of the pharmaceutical composition of the present invention and a pharmaceutical acceptable carrier.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 5 OF 16 USPATFULL on STN
 ACCESSION NUMBER: 2000:54211 USPATFULL
 TITLE: Variants of vascular endothelial cell growth factor
 INVENTOR(S): Keyt, Bruce A., Pacifica, CA, United States
 Nguyen, Francis Hung, Daly City, CA, United States
 Ferrara, Napoleone, San Francisco, CA, United States
 Cunningham, Brian C., San Mateo, CA, United States
 Wells, James A., Burlingame, CA, United States
 Li, Bing, Foster City, CA, United States
 PATENT ASSIGNEE(S): Genentech, Inc., S. San Francisco, CA, United States
 (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6057428 | | 20000502 |
| APPLICATION INFO.: | US 1996-691794 | | 19960802 (8) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. US 1995-567200, filed on 5 Dec 1995 | | |

DOCUMENT TYPE: Utility
 FILE SEGMENT: Granted
 PRIMARY EXAMINER: Feisee, Lila
 ASSISTANT EXAMINER: Kaufman, Claire M.
 NUMBER OF CLAIMS: 20
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 27 Drawing Figure(s); 24 Drawing Page(s)
 LINE COUNT: 3120

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 6 OF 16 USPATFULL on STN
 ACCESSION NUMBER: 2000:12936 USPATFULL
 TITLE: Nucleic acids encoding variants of vascular endothelial cell growth factor
 INVENTOR(S): Keyt, Bruce A., Pacifica, CA, United States
 Nguyen, Francis Hung, Daly City, CA, United States
 Ferrara, Napoleone, San Francisco, CA, United States
 PATENT ASSIGNEE(S): Genentech, Inc., S. San Francisco, CA, United States
 (U.S. corporation)

| | NUMBER | KIND | DATE |
|-----------------------|--|------|--------------|
| PATENT INFORMATION: | US 6020473 | | 20000201 |
| APPLICATION INFO.: | US 1995-567200 | | 19951205 (8) |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | Granted | | |
| PRIMARY EXAMINER: | Spector, Lorraine | | |
| ASSISTANT EXAMINER: | Kaufman, Claire M. | | |
| LEGAL REPRESENTATIVE: | Johnston, Sean, Vance, Dolly A. Flehr Hohbach Test | | |

Albritton & Herbert LLP

NUMBER OF CLAIMS: 8
 EXEMPLARY CLAIM: 1
 NUMBER OF DRAWINGS: 23 Drawing Figure(s); 21 Drawing Page(s)
 LINE COUNT: 2668

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect to binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 7 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2003094617 PCTFULL ED 20031125 EW 200347
 TITLE (ENGLISH): USE OF VEGF FOR TREATING BONE DEFECTS
 TITLE (FRENCH): UTILISATION DE VEGF POUR TRAITER DES DEFAUTS OSSEUX
 INVENTOR(S): BUNTING, Stuart, 220 Miramontes Avenue, Half Moon Bay,
 CA 94019, US;
 FILVAROFF, Ellen Hope, 538 18th Avenue, San Francisco,
 CA 94121, US;
 PEALE, Jr., Franklin V., 416 Pearl Avenue, San Carlos,
 CA 94070, US;
 CARANO, Richard, 2470 Paddock Drive, San Ramon, CA
 94583, US;
 GOSSELIN, Richard Andre, 643 Ferdinand Avenue, El
 Granada, CA 94018, US
 GENENTECH, INC., 1 DNA Way, South San Francisco, CA
 94080-4990, US [US, US]
 CUI, Steven X.\$, GENENTECH, INC., 1 DNA Way, South San
 Francisco, CA 94080-4990\$, US

PATENT ASSIGNEE(S) :

AGENT:

LANGUAGE OF FILING:

LANGUAGE OF PUBL.:

DOCUMENT TYPE:

PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2003094617 | A2 | 20031120 |

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
 CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
 MG MK MN MW MX MZ NI NO NZ OM PH PL PT RO RU SC SD SE
 SG SK SL TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA ZM ZW
 GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (ARIPO) :

AM AZ BY KG KZ MD RU TJ TM

RW (EAO) :

AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU

RW (EPO) :

MC NL PT RO SE SI SK TR

RW (OAPI) :

BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2003-US14090 A 20030506

PRIORITY INFO.:

US 2002-60/378,275 20020506

ABEN The present invention provides pharmaceutical compositions comprising VEGF or variants thereof for promoting bone formation, *<u>in vitro</u>* and *<u>in vivo</u>*. Methods of using those compositions are also provided. Compositions and methods of the present invention can be used

for promoting and improving the repair process in subjects with bone defects.

ABFR L'invention concerne des compositions pharmaceutiques comprenant VEGF ou ses variants, lesquelles compositions permettant de favoriser la formation osseuse, *< i>in vitro</i>* et *< i>in vivo</i>*. L'invention concerne des méthodes d'utilisation de ces compositions. Les compositions et les méthodes de l'invention peuvent être utilisées pour favoriser et pour améliorer le processus de réparation chez des sujets présentant des défauts osseux.

L10 ANSWER 8 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2002083851 PCTFULL ED 20021107 EW 200243
TITLE (ENGLISH): VEGF FUSION PROTEINS
TITLE (FRENCH): PROTEINES DE FUSION VEGF
INVENTOR(S): KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855,
US [US, US];
KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD
21701, US [US, US]
PATENT ASSIGNEE(S): GENVEC, INC., 65 West Watkins Mill Road, Gaithersburg,
MD 20878, US [US, US], for all designates States except
US;
KOVESDI, Imre, 7713 Warbler Lane, Rockville, MD 20855,
US [US, US], for US only;
KESSLER, Paul, D., 1716 Algonquin Road, Frederick, MD
21701, US [US, US], for US only
AGENT: SMITH, Len, S.S., Leydig, Voit & Mayer, Ltd., Suite
4900, Two Prudential Plaza, 180 North Stetson, Chicago,
IL 60601-6780\$, US
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:
NUMBER KIND DATE

WO 2002083851 A2 20021024

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI
SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-US11406 A 20020410

PRIORITY INFO.: US 2001-09/832,355 20010410

ABEN The invention provides therapeutic fusion proteins which include a first peptide portion comprising a first non-heparin binding VEGF peptide portion and a second non-VEGF peptide portion covalently associated with the first peptide portion, which first and second peptide portions separately promote angiogenesis, bone growth, wound healing, or any combination thereof. Further provided are polynucleotides, encoding such fusion proteins, vectors including such polynucleotides, methods of making such proteins, and methods of promoting angiogenesis, bone growth, and/or wound healing using such proteins, polynucleotides, and vectors.

ABFR L'invention concerne des protéines de fusion thérapeutiques comprenant une première partie peptidique renfermant une première partie de peptide VEGF de liaison non héparinique et une seconde partie de peptide non

VEGF associee par covalence a la premiere partie de peptide, lesdites premiere et seconde parties de peptide favorisant separement l'angiogenese, la croissance osseuse, la cicatrisation des blessures ou toute combinaison associee. L'invention concerne en outre des polynucleotides codant pour ces proteines de fusion, des vecteurs comprenant ces polynucleotides, des methodes de fabrication de ces proteines ainsi que des methodes destinees a favoriser l'angiogenese, la croissance osseuse et/ou la cicatrisation des blessures au moyen de ces proteines, ces polynucleotides et ces vecteurs.

L10 ANSWER 9 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2002081520 PCTFULL ED 20021028 EW 200242
 TITLE (ENGLISH): SINGLE CHAIN DIMERIC POLYPEPTIDES
 TITLE (FRENCH): POLYPEPTIDE DIMERIQUE A CHAINE SIMPLE
 INVENTOR(S): BOESEN, Thomas, Peter, Aksel Mollers Have 7, DK-2000
 Frederiksberg, DK [DK, DK];
 HALKIER, Torben, Lyngvej 5, DK-2680 Solrod Strand, DK
 [DK, DK]
 PATENT ASSIGNEE(S): MAXYGEN HOLDINGS LTD., c/o Close Brothers (Cayman)
 Limited, 103 South Church Street, P.O. Box 1034 GT,
 Grand Cayman, KY [—, —], for all
 designates States except US;
 BOESEN, Thomas, Peter, Aksel Mollers Have 7, DK-2000
 Frederiksberg, DK [DK, DK], for US only;
 HALKIER, Torben, Lyngvej 5, DK-2680 Solrod Strand, DK
 [DK, DK], for US only

AGENT: MAXYGEN APS\$, Agern Alle 1, DK-2970 Horsholm\$, DK

LANGUAGE OF FILING: English

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2002081520 | A2 | 20021017 |

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
 CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
 MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI
 SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM ZW
 GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (ARIPO): GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE
 TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2002-DK233 A 20020408

PRIORITY INFO.: DK 2001-PA 2001 00578 20010406

US 2001-60/282,239 20010406

ABEN The invention relates to a single-chain dimeric polypeptide which binds to an extracellular ligand-binding domain of a VEGF type 2 receptor (KDR) or a VEGF type 3 receptor (Flt-4), the polypeptide comprising two receptor-binding sites of which one is capable of binding to a ligand-binding domain of the receptor and one is incapable of effectively binding to a ligand-binding domain of the receptor, and wherein at least one monomer of the dimeric polypeptide is derived from VEGF, VEGF-C or VEGF-D, whereby the single-chain dimeric polypeptide is capable of binding to the receptor, but incapable of activating the receptor. The polypeptide functions as a receptor antagonist for prevention or treatment of a disease or condition involving increased signal transduction from or increased activation of the KDR and/or Flt-4 receptor, e.g. to inhibit angiogenesis or lymphangiogenesis.

ABFR L'invention concerne un polypeptide dimerique a chaîne simple qui se lie à un domaine extracellulaire de liaison aux ligands d'un récepteur VEGF type 2 (KDR) ou d'un récepteur VEGF type 3 (Flt-4), le polypeptide contenant deux sites de liaison aux récepteurs, l'un pouvant se lier à un domaine de liaison aux ligands du récepteur et l'autre ne pouvant pas se lier efficacement à un domaine de liaison aux ligands du récepteur. Au moins un monomère du polypeptide dimerique est dérivé de VEGF, VEGF-C ou VEGF-D, le polypeptide dimerique a chaîne simple pouvant se lier au récepteur mais ne pouvant pas activer le récepteur. Le polypeptide fonctionne comme un antagoniste de récepteur permettant de prévenir ou de traiter une maladie ou un état impliquant une transduction accrue de signal du récepteur KDR et/ou Flt-4 ou une activation accrue du récepteur, notamment pour inhiber une angiogénèse ou une lymphangiogénèse.

L10 ANSWER 10 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2001057067 PCTFULL ED 20020827
 TITLE (ENGLISH): LIGAND FOR VASCULAR ENDOTHELIAL GROWTH FACTOR RECEPTOR
 TITLE (FRENCH): LIGAND DU RECEPTEUR DE FACTEUR DE CROISSANCE
 INVENTOR(S): TCHISTIAKOVA, Lioudmila;
 LI, Shengmin;
 PIETRZYNSKI, Grzegorz;
 ALAKHOV, Valery
 PATENT ASSIGNEE(S): SUPRATEK PHARMA INC.
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2001057067 | A1 | 20010809 |

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL
 SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE
 DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG
 CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:

WO 2001-IB135 A 20010202

PRIORITY INFO.:

US 2000-60/180,568 20000204

ABEN The present invention relates to compositions comprised of a peptide ligand or derivatives thereof that are capable of specific binding to the high affinity receptor-1 of vascular endothelial growth factor (VEGF) and structure similar receptors. The invention further provides a peptide ligand or derivatives thereof that are capable of inhibiting angiogenesis induced by VEGF. The present invention also provides a method for treatment or diagnosis of disease associated with angiogenesis in a patient in need of therapy comprising administering to the patient an effective amount of the pharmaceutical composition of the present invention and a pharmaceutical acceptable carrier.

ABFR L'invention concerne des compositions contenant un ligand peptidique ou des dérivés de celui-ci qui sont capables de se lier spécifiquement au récepteur 1 de grande affinité pour le facteur de croissance endothelial vasculaire (VEGF) et à des récepteurs à structure similaire. L'invention concerne de plus un ligand peptidique ou des dérivés de celui-ci qui sont capables d'inhiber l'angiogénèse induite par VEGF. L'invention concerne aussi une méthode permettant de traiter ou de diagnostiquer une maladie associée à l'angiogénèse chez un patient nécessitant un tel traitement ; cette méthode comprend l'administration au patient d'une quantité efficace de la composition pharmaceutique de l'invention et

d'un excipient pharmaceutiquement acceptable.

L10 ANSWER 11 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2001032695 PCTFULL ED 20020820
 TITLE (ENGLISH): MODULATION OF eNOS ACTIVITY AND THERAPEUTIC USES
 THEREOF
 TITLE (FRENCH): MODULATION DE L'ACTIVITE DE L'eNOS ET SES UTILISATIONS
 INVENTOR(S): SHEN, Ben-Quan;
 ZIONCHECK, Thomas
 PATENT ASSIGNEE(S): GENENTECH, INC.;
 SHEN, Ben-Quan;
 ZIONCHECK, Thomas
 DOCUMENT TYPE: Patent

PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2001032695 | A2 | 20010510 |

DESIGNATED STATES
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
 DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
 CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US30294 A 20001102
 PRIORITY INFO.: US 1999-60/163,132 19991102

ABEN The present invention provides uses of VEGF or VEGF receptor agonists for the up-regulation of eNOS expression and activity. VEGF and VEGF receptor agonists are useful in the treatment of or prevention from hypertension, diabetes, angina, thrombosis, atherosclerosis, heart failure, and other conditions or disorders wherein nitric oxide is an important regulator.

ABFR

L10 ANSWER 12 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 2001012809 PCTFULL ED 20020828
 TITLE (ENGLISH): METHODS AND MEANS FOR INHIBITING ANGIOGENESIS
 TITLE (FRENCH): PROCEDES ET SYSTEMES POUR INHIBER L'ANGIOGENESE
 INVENTOR(S): LEENDERS, Wilhelmus, Petrus, Johannes;
 LUBSEN, Nicolette, Hermance;
 DE WAAL, Robert, Marius, Walther
 INTROGENE B.V.;
 LEENDERS, Wilhelmus, Petrus, Johannes;
 LUBSEN, Nicolette, Hermance;
 DE WAAL, Robert, Marius, Walther
 Patent

PATENT ASSIGNEE(S):
 DOCUMENT TYPE:
 PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2001012809 | A2 | 20010222 |

DESIGNATED STATES
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
 DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG
 CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-NL570 A 20000814
PRIORITY INFO.: EP 1999-99202641.9 19990813

ABEN The present invention discloses heterodimeric VEGF variants with functional VEGF-receptor binding sites at one pole of the asymmetrical dimer, and mutations in the domains for binding to the VEGF tyrosine kinase receptors KDR and Flt-1 at the other pole. These molecules are potent inhibitors of VEGF-induced proliferation and tissue factor induction in endothelial cells and of vascular hyperpermeability.

ABFR

L10 ANSWER 13 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2001009157 PCTFULL ED 20020828
TITLE (ENGLISH): HIGH AFFINITY VASCULAR ENDOTHELIAL GROWTH FACTOR (VEGF)
RECEPTOR NUCLEIC ACID LIGANDS AND INHIBITORS
TITLE (FRENCH): LIGANDS ET INHIBITEURS ACIDE NUCLEIQUE DE RECEPTEUR A
FACTEUR DE CROISSANCE A FORTE AFFINITE VASCULAIRE
ENDOTHELIALE (VEGF)
INVENTOR(S): JANJIC, Nebojsa;
GOLD, Larry
PATENT ASSIGNEE(S): NEXSTAR PHARMACEUTICALS, INC.;
JANJIC, Nebojsa;
GOLD, Larry
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| ----- | | |
| WO 2001009157 | A1 | 20010208 |

DESIGNATED STATES

W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG
CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US20478 A 20000726
PRIORITY INFO.: US 1999-09/364,540 19990729

ABEN Methods are described for the identification and preparation of high-affinity nucleic acid ligands to a VEGF receptor. Included in the invention are specific RNA ligands to a VEGF receptor identified by the SELEX method. Also included are RNA ligands that inhibit the interaction of a VEGF receptor with VEGF.

ABFR

L10 ANSWER 14 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
ACCESSION NUMBER: 2000063380 PCTFULL ED 20020515
TITLE (ENGLISH): VASCULAR ENDOTHELIAL CELL GROWTH FACTOR VARIANTS AND USES THEREOF
TITLE (FRENCH): VARIANTS DU FACTEUR DE CROISSANCE ENDOTHELIALE ET UTILISATIONS CORRESPONDANTES
INVENTOR(S): CUNNINGHAM, Brian;
ABRAHAM, Devos;
LI, Bing
PATENT ASSIGNEE(S): GENENTECH, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|---------|
| ----- | | |
| WO 2000063380 | A1 | 2001026 |

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ
DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS
JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN
MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT
TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW SD SL SZ TZ UG
ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE DK ES FI
FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI CM GA GN
GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2000-US9483 A 20000410

PRIORITY INFO.: US 1999-60/129,788 19990416

US 2000-60/184,235 20000223

ABEN The present invention provides VEGF variants having at least a single amino acid mutation in the native VEGF sequence and selective binding affinity for either the **KDR receptor** or the **FLT-1 receptor**. Methods of making the VEGF variants and methods of using the VEGF variants are also provided.

ABFR La presente invention se rapporte a des variants du VEGF qui presentent au moins une mutation d'acide amine unique dans la sequence du VEGF natif et possedent une affinite de liaison selective soit pour le recepteur KDR soit pour le recepteur FLT-1. L'invention se rapporte egalement a des procedes d'elaboration de ces variants VEGF et a des procedes d'utilisation de tels variants.

L10 ANSWER 15 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN

ACCESSION NUMBER: 1998049300 PCTFULL ED 20020514

TITLE (ENGLISH): TRUNCATED VEGF-RELATED PROTEINS

TITLE (FRENCH): FORMES TRONQUEES DE PROTEINES APPARENTES AU FACTEUR VEGF

INVENTOR(S): BOHLEN, Peter

PATENT ASSIGNEE(S): COLLATERAL THERAPEUTICS

LANGUAGE OF PUBL.: English

DOCUMENT TYPE: Patent

PATENT INFORMATION:

| NUMBER | KIND | DATE |
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| WO 9849300 | A2 | 19981105 |

DESIGNATED STATES

W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE
ES FI GB GE GH GM GW HU ID IL IS JP KE KG KP KR KZ LC
LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT UA UG UZ VN YU ZW GH GM
KE LS MW SD SZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE
CH CY DE DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ
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APPLICATION INFO.: WO 1998-US7801 A 19980420

PRIORITY INFO.: US 1997-08/842,984 19970425

ABEN The present invention provides novel truncated forms of vascular endothelial growth factor-related proteins (VRPs or VRPs) which are useful for the stimulation of angiogenesis *i(in vitro)* and *i(in vivo)*. The invention also provides nucleic acids encoding such novel truncated VRPs and methods of producing truncated VRPs. Pharmaceutical compositions comprising truncated VRPs and methods of gene therapy using the nucleic acids which code for truncated VRPs may be useful for the

ABFR treatment of heart disease and for wound healing.
 Cette invention se rapporte à de nouvelles formes tronquées de protéines apparentées au facteur de croissance endothéliale vasculaire (VRP) qui servent à stimuler l'angiogénèse *in vitro* et *in vivo*). Cette invention se rapporte également à des acides nucléiques codant ces nouvelles protéines VRP tronquées et à des procédés pour produire ces protéines VRP tronquées. Des compositions pharmaceutiques contenant ces protéines VRP tronquées et des procédés de thérapie génétique utilisant les acides nucléiques qui codent ces protéines VRP tronquées peuvent servir dans le traitement des maladies cardiaques et pour la cicatrisation des plaies.

L10 ANSWER 16 OF 16 PCTFULL COPYRIGHT 2004 Univentio on STN
 ACCESSION NUMBER: 1997008313 PCTFULL ED 20020514

TITLE (ENGLISH): VARIANTS OF VASCULAR ENDOTHELIAL CELL GROWTH FACTOR,
 THEIR USES, AND PROCESSES FOR THEIR PRODUCTION
 TITLE (FRENCH): VARIANTS DU FACTEUR DE CROISSANCE DES CELLULES DE
 L'ENDOTHELIUM VASCULAIRE, LEURS UTILISATIONS ET LEURS
 PROCEDES DE FABRICATION

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 FI GB GE HU IL IS JP KE KG KP KR KZ LK LR LS LT LU LV
 MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ
 TM TR TT UA UG US US UZ VN KE LS MW SD SZ UG AM AZ
 BY KG KZ MD RU TJ TM AT BE CH DE DK ES FI FR GB GR IE
 IT LU MC NL PT SE BF BJ CF CG CI CM GA GN ML MR NE SN
 TD TG

APPLICATION INFO.: WO 1996-US13621 A 19960823

PRIORITY INFO.: US 1995-60/002,827 19950825

US 1995-8/567,200 19951205

US 1996-8/691,791 19960802

ABEN The present invention involves the preparation of vascular endothelial growth factor (VEGF) variants which provide materials that are selective in respect of binding characteristics to the kinase domain region and the FMS-like tyrosine-kinase region, respectively KDR and FLT-1. The respective KDR and FLT-1 receptors are bound by corresponding domains within the VEGF compound

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domains. The variants hereof define those two binding regions and modify them so as to introduce changes that interrupt the binding to the respective domain. In this fashion the final biological characteristics of the VEGF molecule are selectively modified.

ABFR La presente invention se rapporte a la preparation de variants du facteur de croissance des cellules de l'endothelium vasculaire (VEGF), lesdits variants constituant des matieres selectives vis a vis des caracteristiques de liaison a la region du domaine kinase (KDR) et a la region tyrosine kinase de type proteine FMS (FLT-1). Les recepteurs respectifs des regions KDR et FLT-1 sont lies par des domaines correspondants a l'interieur des domaines composees du VEGF. Les variants de ce facteur definissent ces deux regions de liaison et les modifient de telle sorte que les modifications introduites interrompent la liaison au domaine respectif. Il est ainsi possible de modifier selectivement les caracteristiques biologiques finales de la molecule du facteur VEGF.

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| FULL ESTIMATED COST | 115.98 | 116.19 |
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